Fig. 1A

A) Before engineering of C_H3 domain

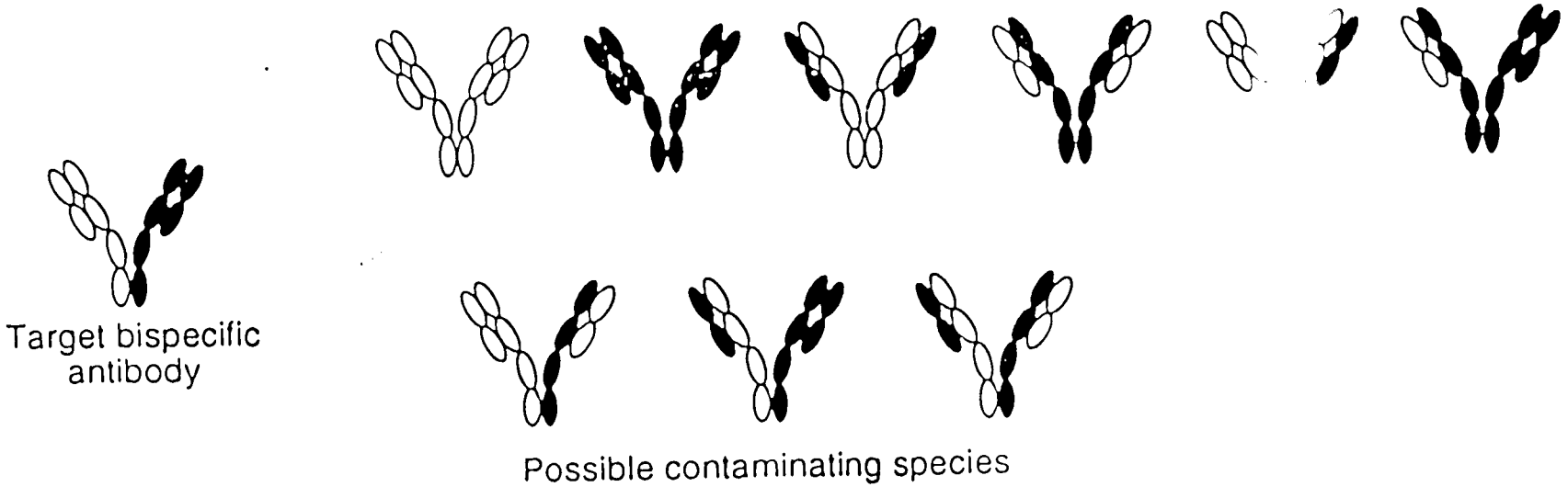
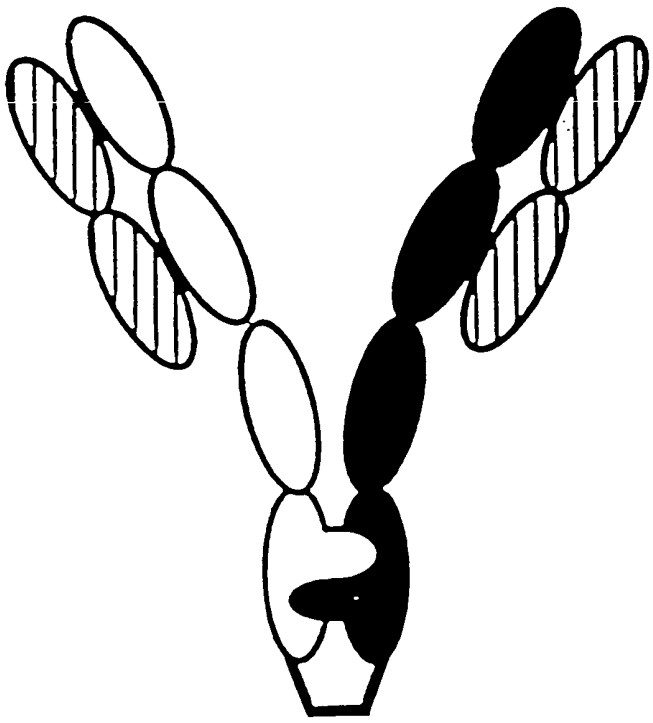


Fig. 1B

B) After engineering of C_H3 domain

∪ = Engineered disulfide bond between CH3 domains



Target bispecific
antibody

Fig. 1C

Fig. 2A

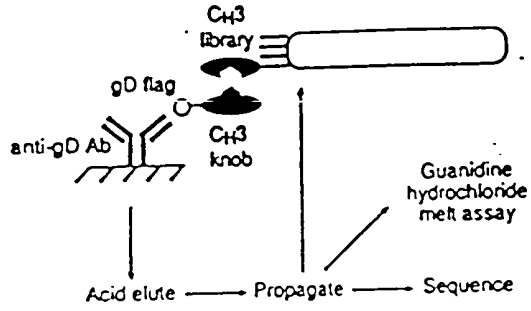


Fig. 2B

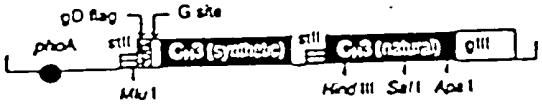
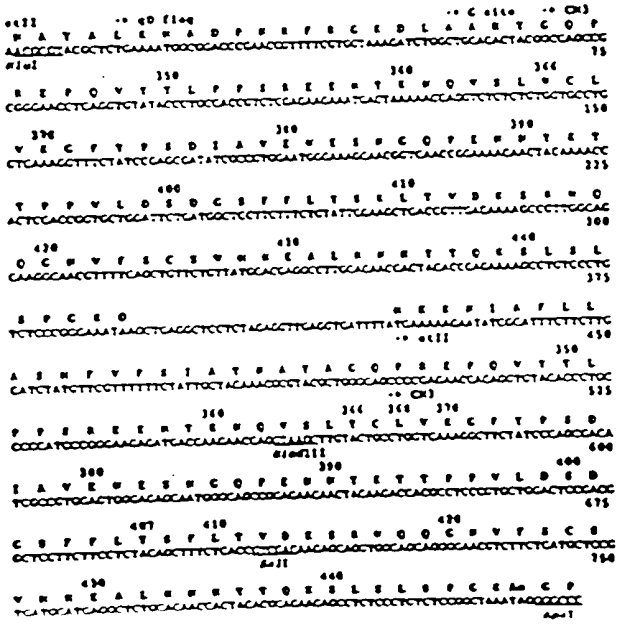


Fig. 2C

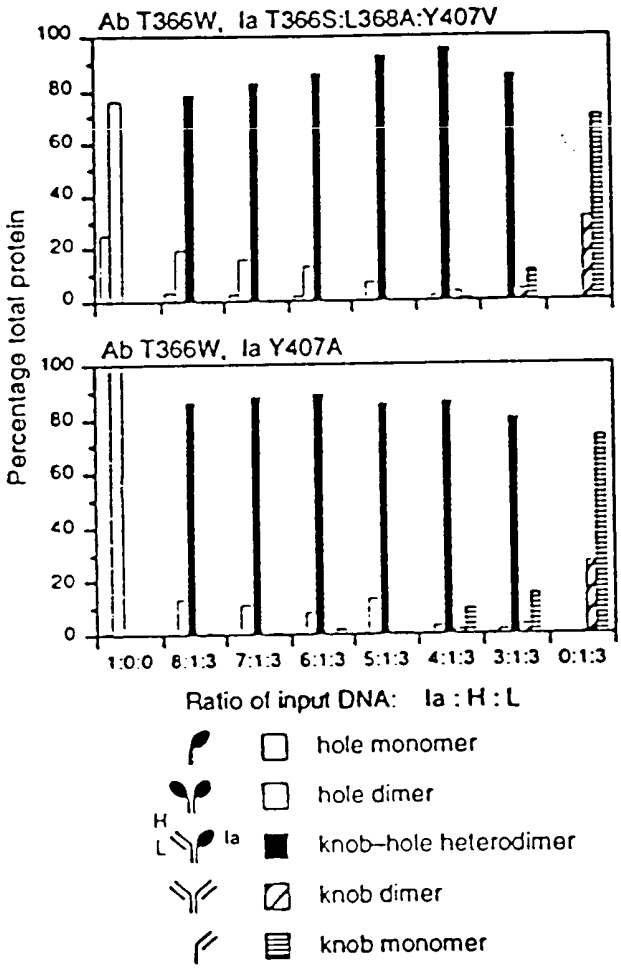


(SEQ ID NO: 13)

Fig. 3A

Fig. 3B

Fig. 3C



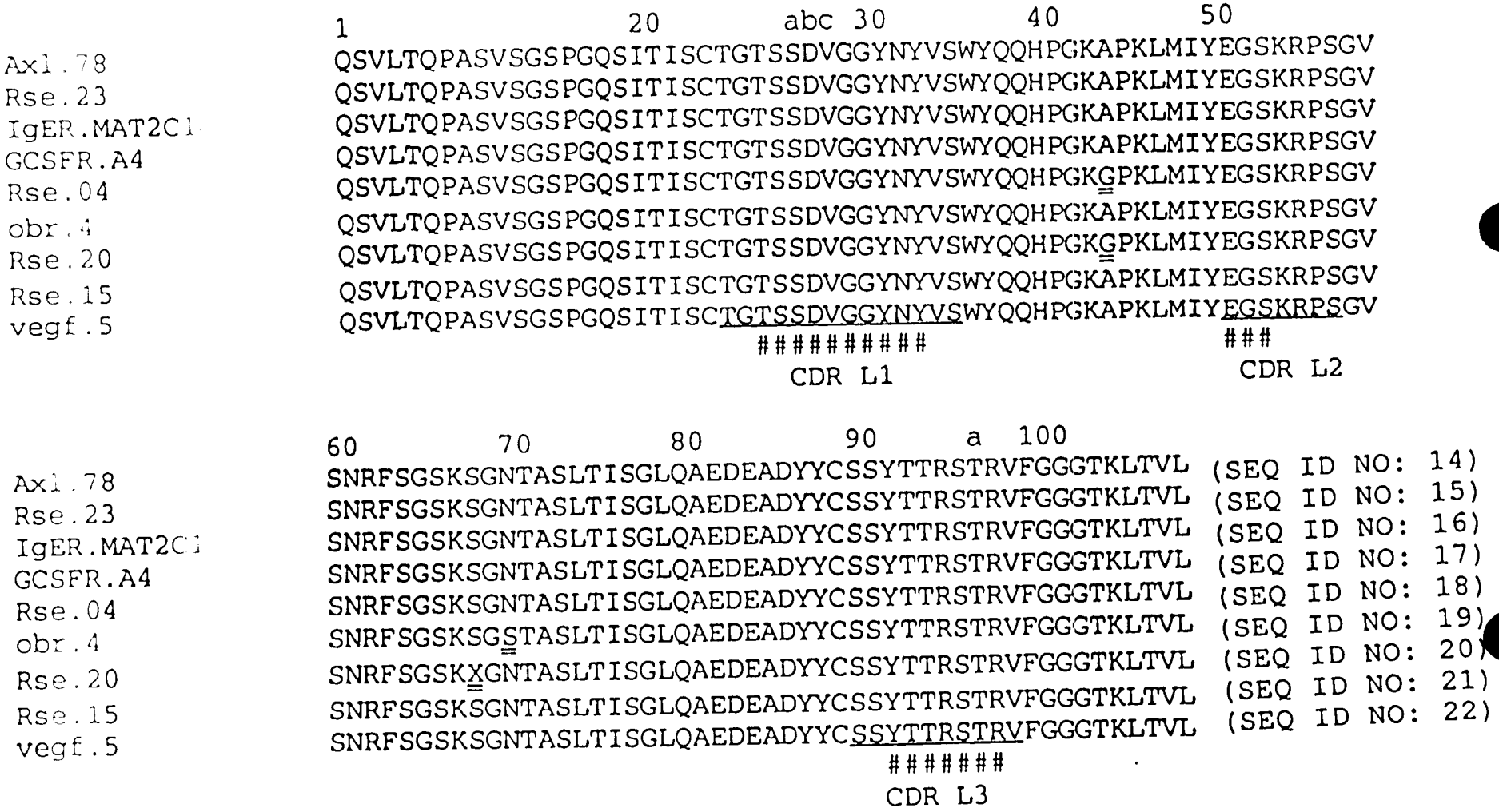

1 20 abc 30 40 50
Axl.78 QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV
Rse.23 QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV
IgER.MAT2C1 QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV
GCSFR.A4 QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV
Rse.04 QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKGPKLMIYEGSKRPSGV
obr.4 QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV
Rse.20 QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKGPKLMIYEGSKRPSGV
Rse.15 QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV
vegf.5 QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV
########## ###
CDR L1 CDR L2
60 70 80 90 a 100
Axl.78 SNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL (SEQ ID NO: 14)
Rse.23 SNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL (SEQ ID NO: 15)
IgER.MAT2C1 SNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL (SEQ ID NO: 16)
GCSFR.A4 SNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL (SEQ ID NO: 17)
Rse.04 SNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL (SEQ ID NO: 18)
obr.4 SNRFSGSKSGSTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL (SEQ ID NO: 19)
Rse.20 SNRFSGSKXGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL (SEQ ID NO: 20)
Rse.15 SNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL (SEQ ID NO: 21)
vegf.5 SNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL (SEQ ID NO: 22)
####### .
CDR L3

Fig. 4

V_H

her3.18 10 20 30 ab 40 50 a

QVQLVQSGGGLVQPGGSLRLSCAASGFTFSSYEMN--WVRQAPGKGLEWVSGISGSGGSTYY

EVQLVESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQHPGKGLEWIGYIY-YSGSTYY

obr.26 CDR H1 CDR H2

60 70 80 abc 90 100abcde 110 (SEQ ID NO: 23)

ADSVKGRFTISRDNSKNTLYLQMNRLRAEDTAVYYCARDNGWELTDWYFDLWGRGTMVTVSS

NPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARVDLEDYGSGASDYWGQGTLVTVSS (SEQ ID NO: 24)

CDR H2 CDR H3

V_L

her3.18 10 20 30 40 50 60

DIQMTQSPSTLSASIGDRVTITCRASEGIYHWLAWYQQKPGKAPKLLIYKASSLASGAPSRF

obr.26 CDR L1 CDR L2

70 80 90 100

SGSGSGTDFTLTISSLQPDDFATYYCQQYSNYPLTFGGGTKLEIK (SEQ ID NO: 25)

CDR L3

Fig. 5

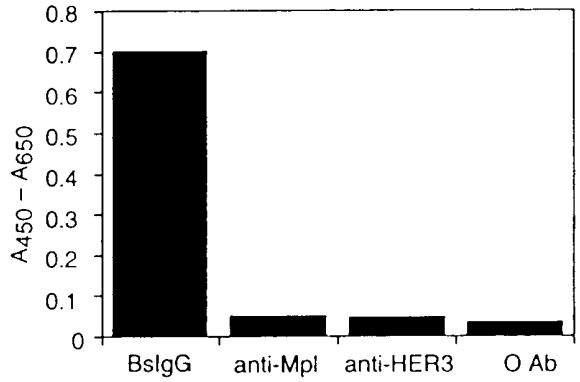
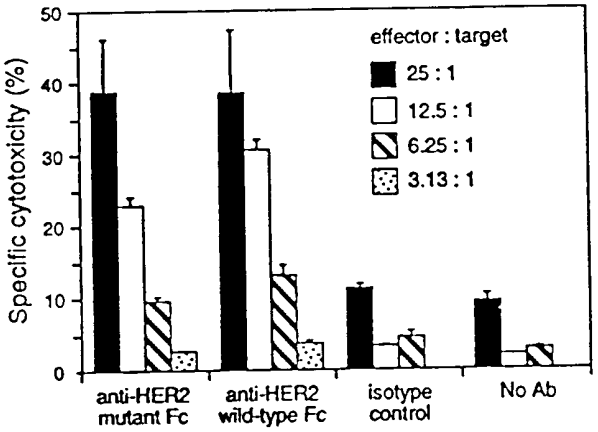


Fig. 6


Specific cytotoxicity (%)
50
40
30
20
10
0
effector : target
25 : 1
12.5 : 1
6.25 : 1
3.13 : 1
anti-HER2 mutant Fc
anti-HER2 wild-type Fc
isotype control
No Ab

Percentage Identity of anti-ObR and anti-HER3 V_L

	H1	H2	H3	H4	H5	H6	H7	H8	H9	H10	H11
O1	49	47	51	81	60	48	76	51	**100**	62	51
O2	84	79	88	50	48	99	48	88	48	45	88
O3	83	82	85	51	50	95	49	85	49	46	85
O4	47	50	51	83	77	48	65	51	73	64	51
O5	49	47	51	81	60	48	76	51	**100**	62	51
O6	83	79	86	50	50	99	47	86	48	45	86
O7	81	**100**	86	51	49	80	48	86	47	44	86
O8	81	**100**	86	51	49	80	48	86	47	44	86
O9	81	**100**	86	51	49	80	48	86	47	44	86
O10	83	79	85	50	49	98	46	85	48	45	85
O11	83	80	87	50	49	99	47	87	48	45	87
O12	81	**100**	86	51	49	80	48	86	47	44	86
O13	49	47	51	81	60	48	76	51	**100**	62	51
O14	50	50	54	95	67	49	76	54	75	62	54
O15	82	79	85	49	48	97	46	85	47	44	85
O16	84	80	87	50	49	**100**	47	87	48	45	87
O17	45	44	47	65	62	45	62	47	62	**100**	47
O18	50	51	50	75	79	50	63	50	66	62	50

O1-018: Anti-Ob-R antibody clones obr. 1, 11, 12, 14, 15, 16, 17, 18, 19, 2, 20, 21, 22, 23, 24, 26, 3, 4, respectively.

H1-H11: Anti-HER3 antibody clones her3.1, 3.10, 3.11, 3.12, 3.16, 3.18, 3.19, 3.22, 3.3, 3.4, 3.7, respectively.

Fig. 8